Therapy of Viral Encephalitis

BETWEEN 1,500 and 3,000 cases of encephalitis are usually reported to the Center for Disease Control in Atlanta each year. In most of these patients no specific etiologic diagnosis can be established; however, postinfectious states, arboviruses and herpes simplex virus account for most of the identifiable causes. The outcome of these illnesses is variable, and depends at least in part on the infecting virus and the age of the patient; however, beween 5 and 10 percent of patients with viral encephalitis die and a less certain percentage are left with permanent neurological disabilities. Because of these hazards there exists considerable interest in the development of some form of effective treatment. The devastating effects of herpes simplex encephalitis (mortality rates between 25 and 50 percent) combined with the availability of several chemotherapeutic agents with *in vitro* efficacy against this virus has led to a number of clinical investigations utilizing these drugs. To date, idoxuridine has been established to be more harmful than beneficial and cytosine arabinoside, which also possesses major toxic effects, has been found to be of questionable value at best. Poly I:C (a complex nucleotide, synthetic polyinosinic-polycytidylic acid), an effective interferon inducer, has also been tried but offers little hope because of its adverse effects. Adenine arabinoside is currently being tested, and the question of its effectiveness awaits the outcome of controlled studies.

No specific therapy is available for arboviruses, but interferon and its inducers have been shown to be effective against experimental arbovirus infections when given before or shortly after the administration of virus. No extensive clinical trials of the substances have been undertaken.

Lastly, postinfectious encephalitis, usually associated with mumps, measles or chicken pox, may well be mediated in many cases by conditions other than direct viral invasion of the brain. Many investigators feel immunological phenomenon may be important in these disease processes. No antiviral agent has been shown effective in these disorders.

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Mitral Valve Prolapse

MITRAL VALVE PROLAPSE is the most common cause of mitral regurgitation. Although prolapse may result from or be associated with Marfan's syndrome, ischemic heart disease, atrial septal defect and hypertrophic cardiomyopathy, there is no identifiable cause in most involved patients. Myxomatous degeneration of the mitral (and occasionally the tricuspid) valve is commonly present in this syndrome.

Auscultation of a variable midsystolic click or late systolic murmur, or both, strongly suggests the diagnosis. Examination during postural maneuvers may intensify or clarify the pathological findings. When the patient squats, the click moves toward the second sound and the murmur is abbreviated and softened. Standing after squatting moves the click toward the first sound, and greatly intensifies and lengthens the murmur.

Most patients are asymptomatic. However, there is a subset of subjects with mitral valve prolapse in whom both symptoms and associated abnormalities are present. A clinician should suspect prolapse when confronted with a young, often anxious, thin patient complaining of fatigue and chest pain or palpitations, or both. Women outnumber men two to one among these patients. Bony abnormalities such as kyphoscoliosis, pectus excavatum and "straight back syndrome" are common. On electrocardiograms, inferior lead T wave inversion, prolonged Q-T interval and frequent atrial or ventricular premature beats may be seen. Exercise may cause ST segment depression and increase the frequency of premature beats, especially after the exercise. Rarely, a life-threatening arrhythmia such as ventricular tachycardia occurs; ventricular fibrillation and sudden death have been reported.

Findings on echocardiography may be diagnostic, showing there to be systolic posterior excursion of one or both mitral leaflets. Cardiac catheterization is rarely indicated for diagnosis, but if the characteristic leaflet billowing is shown to exist and coronary arteries are judged by angiography to be normal, these may help establish that coronary obstruction is not causing the patient's chest pain.

Antibiotic prophylaxis is indicated for dental or potentially contaminated surgical procedures. Propranolol, 40 to 320 mg per day, should be used for symptomatic or life-threatening arrhythmias. Refractory ventricular arrhythmias have

been controlled by atrial overdrive pacing and mitral valve replacement.

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Treatment of Myxedema and Myxedema Coma

EXCEPT FOR myxedema coma, there are few situations in which hypothyroidism requires rapid restoration of the eumetabolic state. Hypothyroid patients are sensitive to thyroid hormone replacement, even at low doses and, therefore, therapy should be initiated at a dosage of no more than 50 μg of levothyroxine per day. In patients with underlying heart disease or severe hypothyroidism the initial daily dose should be even lower. The dose should then be increased by 25 to 50 μg at two- to four-week intervals until a normal metabolic state is reached. The final maintenance dose should be approximately 200 μg per day.

Occasionally, cardiovascular or psychiatric complications limit the use of the full therapeutic dose and replacement therapy must be modified to attain the maximal metabolic state without adverse effects.

The clinical state of the patient is generally the best determinant of adequate thyroid hormone replacement. The wide range of normal for thyroxine (T_4) concentration makes the T_4 determination useful only as a confirmation of a patient's metabolic state. In a patient with thyroprival hypothyroidism, thyroid-stimulating hormone (TSH) determinations can be used to assess the patient's response to thyroid hormone replacement.

Although levothyroxine appears to be the agent of choice in replacement therapy of hypothyroidism, for those who prefer other agents the equivalent doses are levothyroxine, 100 μg; liothyronine, 25 μg, and thyroid extract, 60 mg.

The severity of myxedema coma requires that the diagnosis be made clinically and therapy begun immediately. Therapy should be initiated with 400 to 500 μg of levothyroxine given intravenously. Respiratory care is critical and hypoventilation should be treated by assisted ventilation and controlled oxygen administration. The occasional associated hypoglycemia should be treated with concentrated glucose solutions to avoid water intoxication. Dilutional hyponatremia should be treated by water restriction but may occasionally require hypertonic saline infusion. Hydrocortisone, 100 to 200 mg per day, should be administered intravenously. The patient should not be actively warmed. Precipitating factors such as infection should be sought and treated.

Although myxedema coma generally has a poor prognosis, a regimen such as the above, especially with critical attention to respiratory care and ideally in the setting of an intensive care unit, should increase survivals.

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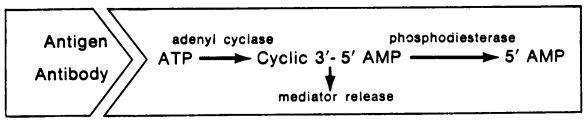
Bronchodilator Pharmacology

ALTHOUGH A VARIETY of catecholamine and xanthine preparations have been used for the treatment of asthma and other types of airway obstruction for many years, only recently has the mechanism of action of these agents become appreciated. An understanding of bronchodilator pharmacology has led to the rational use of these agents and has given impetus to the search for additional agents with greater specificity of action.

The airway obstruction of acute bronchial asthma is due, at least in part, to the release of several biologically active substances, as shown in a simplified diagram in Figure 1.



AMP = adenosine monophosphate
ATP = adenosine triphosphate

Figure 1.—Diagram showing release of biologically active substances.